10

15

20

25

30

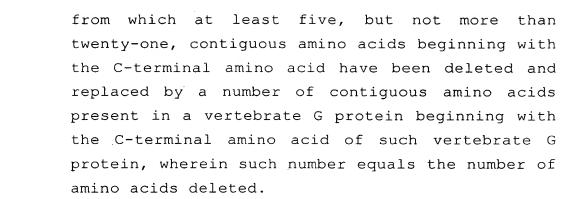
35



What is claimed is:

1. An isolated nucleic acid encoding a chimeric G protein, wherein the chimeric G protein comprises an invertebrate $G\alpha q$ G protein from which at least five, but not more than twenty-one, contiguous amino acids beginning with the C-terminal amino acid have been deleted and replaced by a number of contiguous amino acids present in a vertebrate G protein beginning with the C-terminal amino acid of such vertebrate G protein, wherein such number equals the number of amino acids deleted or varies therefrom by no more than five amino acids, provided that at least five of the Cterminal amino acids of the chimeric G protein are present at the C-terminus of such vertebrate G protein.

- A nucleic acid of claim 1, wherein the chimeric G 2. protein comprises an invertebrate $G\alpha q$ G protein from which at least five, but not more than twenty-one, contiquous amino acids beginning with the C-terminal amino acid have been deleted and replaced by a number of contiguous amino acids present in a vertebrate G protein beginning with the C-terminal amino acid of such vertebrate G protein, wherein such number equals the number of amino acids deleted or varies therefrom by no more than two amino acids, provided that at least the C-terminal amino acids five of chimeric G protein are present at the C-terminus of such vertebrate G protein.
- 3. A nucleic acid of claim 1, wherein the chimeric G protein comprises an invertebrate $G\alpha q$ G protein



- 10 4. The nucleic acid of claim 1, wherein the nucleic acid is DNA.
 - 5. The nucleic acid of claim 4, wherein the DNA is cDNA.
 - 6. The nucleic acid of claim 4, wherein the DNA is genomic DNA.
- 7. The nucleic acid of claim 1, wherein the nucleic acid is RNA.
 - 8. The nucleic acid of claim 1, wherein the vertebrate G protein is a mammalian G protein.
- 9. The nucleic acid of claim 1, wherein the contiguous amino acids which have been deleted are contained in FVFAAVKDTILQHNLKEYNLV* (SEQ ID NO: 37), wherein V* is the C-terminal amino acid.
- 30 10. The nucleic acid of claim 1, wherein the vertebrate G protein is a vertebrate $G\alpha z$ G protein.
- 11. The nucleic acid of claim 10, wherein the number of contiguous amino acids which have replaced the deleted amino acids are contained in

10

15

20

25

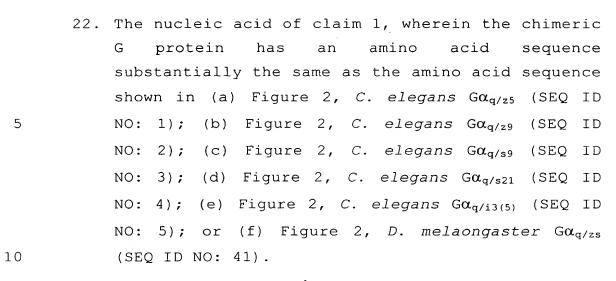


FVFDAVTDVIIQNNLKYIGLC* (SEQ ID NO: 38), wherein C* is the C-terminal amino acid.

- 12. The nucleic acid of claim 10, wherein the invertebrate $G\alpha q$ G protein has five contiguous amino acids beginning with the C-terminal amino acid which have been deleted and replaced by five contiguous amino acids beginning with the C-terminal amino acid of the vertebrate $G\alpha z$ protein.
 - 13. The nucleic acid of claim 1, wherein the vertebrate G protein is a vertebrate $G\alpha s$ G protein.
- 14. The nucleic acid of claim 13, wherein the number of contiguous amino acids which have replaced the deleted amino acids are contained in RVFNDCRDIIQRMHLRQYELL* (SEQ ID NO: 39), wherein L* is the C-terminal amino acid.
 - 15. The nucleic acid of claim 13, wherein the invertebrate $G\alpha q$ G protein has nine contiguous amino acids beginning with the C-terminal amino acid which have been deleted and replaced by nine contiguous amino acids beginning with the C-terminal amino acid of the vertebrate $G\alpha s$ protein.
- 30 16. The nucleic acid of claim 1, wherein the vertebrate G protein is a vertebrate $G\alpha$ i3 G protein.
- 17. The nucleic acid of claim 16, wherein the number of contiguous amino acids which have replaced the

deleted amino acids are contained in FVFDAVTDVIIKNNLKECGLY* (SEQ ID NO: 40), wherein Y* is the C-terminal amino acid.

- 5 18. The nucleic acid of claim 16, wherein invertebrate Gaq G protein has five contiquous amino acids beginning with the C-terminal amino acid which have been deleted and replaced by five contiguous amino acids beginning with the C-10 terminal amino acid of the vertebrate $G\alpha i3$ protein.
- 19. The nucleic acid of claim 1, wherein the vertebrate G protein is a vertebrate Gαil G protein, a vertebrate Gαi2 G protein, a vertebrate GαoA G protein, or a vertebrate GαoB G protein.
- 20. The nucleic acid of claim 1, wherein the invertebrate $G\alpha q$ G protein is a Caenorhabditis elegans $G\alpha q$ G protein.
- 21. The nucleic acid of claim 1, wherein invertebrate $G\alpha q$ G protein is a Drosophila 25 melanogaster $G\alpha q$ G protein, a Limulus polyphemus $G\alpha q$ G protein, a Patinopecten yessoensis $G\alpha q$ G protein, а Loligo forbesi Gag G protein, a Homarus americanus Gaq G protein, a stagnalis Gag G protein, a Geodia cydonium Gag G 30 or a Dictyostelium discoideum Ga4 G protein, protein.



- 23. A vector comprising the nucleic acid of claim 1.
- 24. A vector of claim 28 adapted for expression in a cell which comprises the regulatory elements necessary for expression of the nucleic acid in the cell operatively linked to the nucleic acid encoding the chimeric G protein so as to permit expression thereof, wherein the cell is a bacterial, amphibian, yeast, insect, or mammalian cell.
 - 25. The vector of claim 21, wherein the vector is a plasmid, a baculovirus or a retrovirus.
 - 26. A cell comprising the vector of claim 23, wherein the cell comprises DNA encoding a mammalian G protein-coupled receptor.
- 27. A cell of claim 26, wherein the DNA encoding the mammalian G protein-coupled receptor is endogenous to the cell.

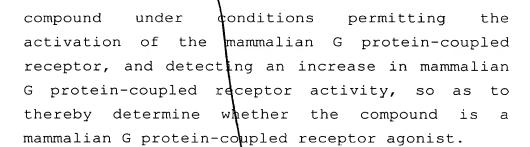
25

30

- 28. A cell of claim 26, wherein the DNA encoding the mammalian G protein-coupled receptor is transfected into the cell.
- 5 29. A cell of claim 26, wherein the cell is a non-mammalian cell.
 - 30. A cell of claim 29, wherein the non-mammalian cell is a *Xenopus* pocyte cell or a *Xenopus* melanophore cell.
 - 31. A cell of claim 26, wherein the cell is a mammalian cell.
- 32. A mammalian cell of claim 31, wherein the cell is a COS-7 cell, a 293 human embryonic kidney cell, a NIH-3T3 cell, a LM(tk-) cell, a mouse Y1 cell, or a CHO cell.
- 20 33. A cell of claim 26 wherein the cell is an insect cell.
 - 34. An insect cell of claim 33,\ wherein the insect cell is an 3f9 cell, an Sf21 cell or a Trichoplusia n = 5B-4 cell.
 - 35. A membrane preparation isolated from the cell of any one of claims 26, 27, 28, 29, 31, 32, 33 or 34.
 - 36. A process for determining whether a chemical compound is a mammalian G protein-coupled receptor agonist which comprises contacting cells transfected with and expressing DNA encoding a chimeric G protein and expressing DNA encoding a mammalian G protein-coupled receptor, with the

10

15

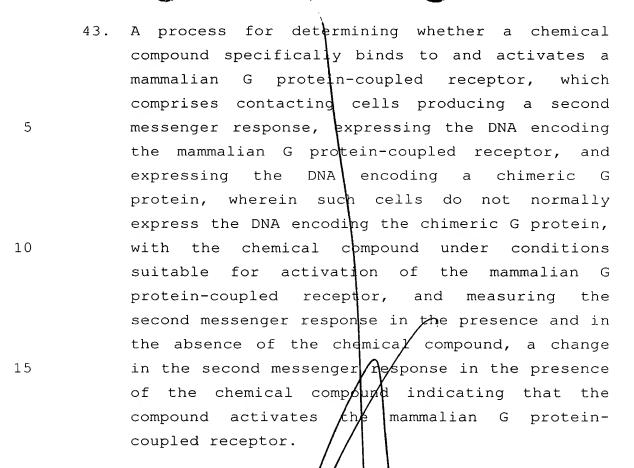


- 37. A process for determining whether a chemical compound is mammalian G protein-coupled а receptor agonist which comprises contacting a membrane preparation from cells transfected with and expressing DNA encoding a chimeric G protein expressing encoding a mammalian DNA protein-coupled receptdr, with the compound under conditions permitting the activation of the mammalian G prote/In/coupled receptor, and i/h mammalian G proteindetecting an increase coupled receptor a¢ti√jit∫y, so as to thereby determine whether the combound is a mammalian G protein-coupled receptor agonist.
- determining whether a chemical 38. A process for compound is mammaliah G protein-coupled receptor antagdnist which comprises contacting transfected 25 with and expressing encoding a chimeric G protein and expressing DNA encoding a mammalian G protein-coupled receptor, with the compound in the presence of a mammalian G protein-coupled receptor agonist, under conditions permitting the activation of 30 the mammalian G protein-coupled receptor, detecting a decrease in mammalian G proteincoupled receptor activity, so as to thereby determine whether the compound is a mammalian G 35 protein-coupled receptor antagonist.

10

15

- 39. A process for determining whether a chemical compound is mammalian G protein-coupled a receptor antagonist which comprises contacting a membrane preparation from cells transfected with and expressing DNA encoding a chimeric G protein expressing DNA encoding a mammalian G protein-coupled receptor, with the compound in the presence of a khown mammalian G proteincoupled receptor adonist, under conditions permitting the activation of the mammalian G protein-coupled receptor, and detecting decrease in mammalian & protein-coupled receptor activity, so as to thereby determine whether the mammalian G protein-coupled compound is a receptor antagonist.
- 40. The process of claim 36, 37, 38, or 39, wherein the DNA encoding the mammalian G protein-coupled receptor is endogenous to the cell.
- 41. The process of claim 36, 37, 38, or 39, wherein the DNA encoding the mammalian G protein-coupled receptor is transfected into the cell.
- The process of daim 36, 37, 38, or 39, wherein 25 42. the mammalian of protein-coupled receptor is a human Y5 receptor, a human GALR2 receptor, a kappa opioid receptor, human a human receptor, a human NPFF2 receptor, a human α2A 30 adrenergic receptor, þ human dopamine D2 receptor, a human GALR1 receptor, a human Y2 receptor, a human Y1 receptor, а human Y 4 receptor, a human α 1A adrenergic receptor, a human dopamine D1 receptor, or rat NTR1 a 35 receptor.



- 20 44. The process of claim 43, wherein the DNA encoding the mammalian G protein coupled receptor is endogenous to the gelt.
- 45. The process of claim 43, wherein the DNA encoding
 the mammalian 5 protein-coupled receptor is
 transfected into the cell.
- 46. The process of claim 43, wherein the second messenger response is the detection of a reporter protein under the transcriptional control of a promoter element.
 - 47. The process of claim 43, wherein the second messenger response is measured by a change in cell proliferation.

25

30

- 48. The process of claim 43, wherein the second messenger response is a $G\alpha q$ second messenger response.
- 5 49. The process of claim 48, wherein the $G\alpha q$ second messenger response comprises release of inositol phosphate and the change in second messenger is an increase in the level of inositol phosphate.
- 10 The process of claim 48, wherein the $G\alpha q$ second 50. messenger response comprises release of arachidonic acid and the change in second messenger is in the an increasa level of arachidonic acid.
- The process of claim /48, wherein the G α q second 51. messenger responsé comprises activation of MAP kinase and the **c**ha**h**ge in second messenger response is increase MAP an/ in kinase 20 activation.
 - The process bf/claim 48 wherein the Gag second 52. response comprises messenger intracellular calcium lev∉ls th/e and change in second L's an inchease messenger in the measure of intracellular calcium.
 - 53. The process of claim \$2, wherein the measure of intracellular calcium levels is made by chloride current readings.
 - 54. The process of claim 52, wherein the measure of intracellular calcium is made by fluorescence readings, luminescence readings, electrophysiological readings, or through the

10

15

20

25

30

detection of a reporter protein under the transcriptional control of a calcium-responsive promoter element.

- 55. A process for determining whether a chemical compound specifically binds to and a mammalian activation of G protein-coupled receptor, which comphises separately contacting cells producing a second messenger response, encoding the mammalian G expressing the DNA protein-coupled receptor, and/expressing the DNA a chimeric G protein, encoding wherein cells do not normally express the DNA encoding the chimeric G protein, with both the chemical compound and a second dhemical compound known to activate the mammalian protein-coupled G receptor, and with phly. the second chemical compound, under donditions suitable mammalian G protein-coupled activation of t/he measuring and the second messenger of only the second response in the presence chemical compound/and **i**|n the presence of both the second chemical compound and the chemical compound, a smaller change in the second messenger response in the presence of both the compound the chemical and second compound than in the presence of only the second chemical compound indicating that the chemical compound inhibits activation of the mammalian G protein-coupled receptor.
 - 56. The process of claim 55, wherein the DNA encoding the mammalian G protein-coupled receptor is endogenous to the cell.

- 57. The process of claim 55, wherein the DNA encoding the mammalian G protein-coupled receptor is transfected into the cell.
- 5 58. The process of claim 55, wherein the second messenger response is the detection of a reporter protein under the transcriptional control of a promoter element.
- 10 59. The process of claim 55, wherein the second messenger response is measured by a change in cell proliferation.
- 60. The process of claim 55, wherein the second messenger response is a $G\alpha q$ second messenger response.
 - 61. The process of claim 60, wherein the Gαq second messenger response comparises release of inositol phosphate and the change in second messenger response is a smaller increase in the level of inositol phosphate in the presence of both the chemical compound and the second chemical compound than in the presence of only the second chemical compound.
 - 62. The process of claim 60, wherein the $G\alpha q$ second messenger response comprises activation of MAP kinase and the change in second messenger response is a smaller increase in the level of MAP kinase activation in the presence of both the chemical compound and the second chemical compound than in the presence of only the second chemical compound.

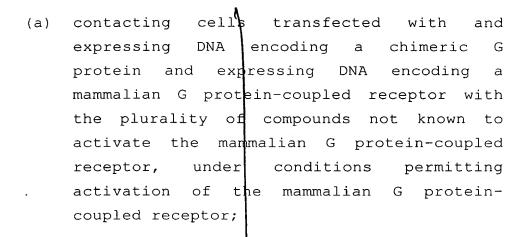
30

20

30

35

- The process of claim 60, wherein the $G\alpha q$ second messenger response comprises release ofarachidonic acid and the change in second messenger response is an increase in the level of arachidonic acid levels in the presence of the chemical compound and the chemical compound than in the presence of only the second chemical dompound.
- 10 64. The process of claim 60, wherein the Gαq second messenger response comprises change in intracellular calcium levels and the change in second messenger response is a smaller increase in the measure of intracellular calcium in the presence of both the chemical compound and the second chemical compound than in the presence of only the second chemical compound.
- 65. The process of claim 64, wherein the measure of intracellular calcium levels is made by chloride current readings
 - 66. The process of claim 64, wherein the measure of intracellular datcium is made by fluorescence readings, luminescence readings, electrophysiological readings, or through the detection of a reporter protein under the transcriptional control of a calcium-responsive promoter element.
 - 67. A process of screening a plurality of chemical compounds not known to activate a mammalian G protein-coupled receptor to identify a compound which activates the mammalian G protein-coupled receptor which comprises:



(b) determining whether the activity of the mammalian G protein-coupled receptor is increased in the presence of one or more of the compounds; and if so

(c) separately determining whether the activation of the mammalian G protein-coupled receptor is increased by any compound included in the plurality of compounds, so as to thereby identify each compound which activates the mammalian G protein-coupled receptor.

68. A process of screening a plurality of chemical compounds not known to inhibit the activation of a mammalian G protein-coupled receptor to identify a compound which inhibits the activation of the mammalian G protein-coupled receptor, which comprises:

(a) contacting cells transfected with and expressing DNA encoding а chimeric protein and expressing DNA encoding mammalian G protein-coupled receptor with the plurality of compounds in the presence of known mammalian G protein-coupled

30

5

10

15

20

25

protein-coupled receptor;

5

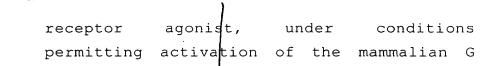
10

15

20

25

30



- (b) determining whether the extent or amount of activation of the mammalian G protein-coupled receptor is reduced in the presence of one or more of the compounds, relative to the extent or amount of activation of the mammalian G protein-coupled receptor in the absence of such one or more compounds; and if so
 - separately determining whether (C) each such inhibits / activation compound of the G protein-coupled receptor mammalian each compound in ded in the plurality of compounds, so/ a/s to thereby identify any indluded in such plurality of compound compounds which inhibits the activation of the mammalian G protein-coupled receptor.
- 69. The process of dlaim 67 or 68, wherein the DNA encoding the mammalian G protein-coupled receptor is endogenous to the cell.
- 70. The process of claim 67 or 68, wherein the DNA encoding the mammalian G protein-coupled receptor is transfected into the cell.
- 71. A process for determining whether a chemical compound is a mammalian G protein-coupled receptor agonist, which comprises separately contacting membrane preparations from cells transfected with and expressing DNA encoding a chimeric G protein and expressing DNA encoding a

mammalian G protein-doupled receptor with both [^{β5}S]GTPγS, compound and and with the only [35S]GTPyS, under conditions permitting activation of the mammalian G protein-coupled receptor, and detecting [35S]GTPyS binding to the membrane preparation and an increase in [35S]GTPγS bindina in the presence of the indicating that the chemical compound activates the mammalian G protein-coupled receptor.

10

15

20

25

5

72. A process for determining whether a chemical protein-coupled is а mammaliap-G compound which comprises separately receptor antagonist preparations from contacting membrane transfected with and encoding a chimeric G protein and expressing DNA encoding a mammalian G protein-fourled receptor with the compound, $[^{35}$]$ GTP γ S, and chemical а second chemical compound known to activate the mammalian G protein-coupled/receptor, with [35S]GTPyS and second compound, and with [35S]GTPyS only the alone, under conditions permitting the activation of the mammalian G protein-coupled receptor, detecting $/[^{35}\beta]$ GTP γ S binding to each membrane preparation,/comparing the increase in [35S]GTPyS binding in the presence of the compound and the compound relative to the binding [35S]GTPyS alone to the increase in [35S]GTPyS binding in the presence of the second chemical compound relative $t\phi$ the binding of [35 S]GTPyS and detecting a alone, smaller increase [35S]GTPyS binding in the presence of the compound and the second compound indicating that mammalian G protein-coupled compound i s а receptor antagonist.

35

35

5

- 73. The process of claim 71 or 72, wherein the DNA encoding the mammalian G protein-coupled receptor is endogenous to the cell.
- 74. The process of claim 71 or 72, wherein the DNA encoding the mammalian G protein-coupled receptor is transfected into the cell.
- 75. The process of claim 71 or 72, wherein the mammalian G protein-coupled receptor produces a Gas second messenger response in the absence of the chimeric G protein
- 76. A process for determining whether a chemical 15 mamma**l/**ian compound is а G protein-coupled receptor agonist, whith comprises contacting transfected wi/#h cells and expressing encoding a chimeric G/protein and expressing DNA 20 encoding a mammalian $/ f \setminus p$ rotein-coupled receptor with a compound, und $\notin t$ donditions permitting the the mammalian G protein-coupled activation of detecting changes receptor, and in receptor conformation as manifested active state 25 receptor/G changes in protein heterotrimer association/dissociation in the presence of the compound indicating that the chemical compound protein-coupled activates the mammalian G

receptor.

77. A process for determining whether a chemical compound is a mammalian G protein-coupled receptor antagonist which comprises separately contacting cells transfected with and expressing DNA encoding a chimeric G protein and expressing DNA encoding a mammalian G protein-coupled

. 5

10

15

35

chemical compound in with the presence of a known mammalian G protein-coupled agonist/ under conditions permitting the mammalian G proteinactivation / of and detecting changes coupled receptor, receptor active state conformation as manifested by changes in receptor/G protein heterotrimer association/dissociation in the presence of the that compound indicating the compound is a mammalian G protein-coupled receptor antagonist.

- 78. The process of claim 76 or 77, wherein the DNA encoding the mammalian G protein-coupled receptor is endogenous to the cell.
- 79. The process of claim 6 or 77, wherein the DNA encoding the mammalian G protein-coupled receptor is transfected into the cell.
- The process of any one of claims 36, 37, 38, 39, 20 71, 43, 55, 67, 68, 2, 76, or 77, wherein the chimeric G protein comprises an invertebrate Gαq G protein from which at least five, but not more than twenty-one, contiguous amino acids beginning 25 with the C-terminal amino acid have been deleted and replaced by a number of contiguous amino acids present/in a vertebrate G protein beginning with the C-terminal amino acid of such vertebrate G protein, wherein such number equals the number of amino acids deleted. 30
 - 81. The process of any one of claims 36, 37, 38, 39, 43, 55, 67, 68, 71, 72, 76, or 77, wherein the chimeric G protein comprises an invertebrate $G\alpha q$ G protein from which at least five, but not more than twenty-one, contiguous amino acids beginning

10

15

35

with the C-terminal amino acid have been deleted and replaced by a number of contiguous amino acids present in a vertebrate $G\alpha z$ protein beginning with the C-terminal amino acid of such vertebrate $G\alpha z$ protein, wherein such number equals the number of amino acids deleted.

- 82. The process of any one of claims 36, 37, 38, 39, 43, 55, 67, 68, 71, 72, 76, or 77, wherein the chimeric G protein comprises an invertebrate $G\alpha q$ G protein from which at least five, but not more than twenty-one, contiguous amino acids beginning with the C-terminal amino acid have been deleted and replaced by a humber of contiguous amino present in ve**f**tebrate $G\alpha s$ acids protein beginning with the C-term/nal amino acid of such vertebrate $G\alpha s$ protein/ wherein such equals the number of ami/no acids deleted.
- 83. The process of any one of claims 36, 37, 38, 39, 20 43, 55, 67, 68, 71/ 2, 76, or 77, wherein the chimeric G protein/c/mprises an invertebrate $G\alpha q$ G protein from which at least five, but not more than twenty-one, contiguous amino acids beginning 25 with the C-terminal amino acid have been deleted and replaced by a number of contiguous amino acids present $/\!\!\!/$ n a $/\!\!\!\!/$ ertebrate G α i3 beginning with the C-terminal amino acid of such vertebrate Gαi# protein \ wherein such number 30 equals the number of amino acids deleted.
 - 84. The process of any one of claims 36, 37, 38, 39, 43, 55, 67, 68, 71, 72, 76, or 77, wherein the chimeric G protein comprises a *Caenorhabditis* elegans Gαq G protein from which at least five,

10

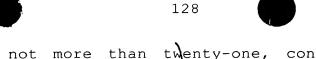
15

20

25

30

35

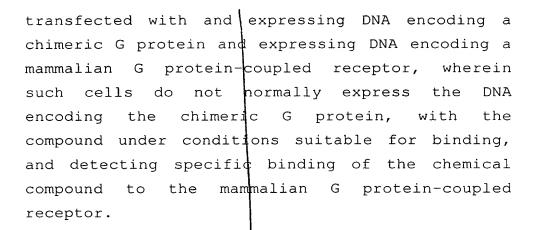


but not more than twenty-one, contiguous amino acids beginning with the C-terminal amino acid have been deleted and replaced by a number of contiguous amino acids present in a vertebrate G protein beginning with the C-terminal amino acid of such vertebrate G protein, wherein such number equals the number of amino acids deleted.

- The process of any one of claims 36, 37, 38, 39, 43, 55, 67, 68, 71, 72, 76, or 77, wherein the protein comprises a Drosophila chimeric G melanogaster Gaq G protein, a Limulus polyphemus Gαq G protein, a Patihopecten yessoensis Gαq G forbesi Gαq G protein, a protein, a Loligo Homarus americanus Gαq G/ protein, а stagnalis Gαq G protein, A Geodia cydonium Gαq G protein, or a Dictyost/elium discoideum G $lpha_4$ G protein, from which at least five, but not more than twenty-one, contiguous amino acids beginning with the C-termina/1 a/mino acid have been deleted and replaced by / a /number of contiguous amino acids present in/a vertebrate G protein beginning with the C-term‡na¼ amino acid of a vertebrate G protein, wherein such number equals the number of amino acids deleted.
- 86. The process of any one of claims 36, 37, 38, 39, 43, 55, 67, 68, 71, 72, 76, or 77, wherein the chimeric G protein has an amino acid sequence substantially the same as the amino acid sequence shown in (a) Figure 2, C. elegans $G\alpha_{q/z5}$ (SEQ ID NO: 1); (b) Figure 2, C. elegans $G\alpha_{q/z9}$ (SEQ ID NO: 2); (c) Figure 2, C. elegans $G\alpha_{q/s9}$ (SEQ ID NO: 3); (d) Figure 2, C. elegans $G\alpha_{q/s21}$ (SEQ ID NO: 4); (e) Figure 2, C. elegans $G\alpha_{q/i3(5)}$ (SEQ ID

NO: 5); or (f) Figure 2, D. melaongaster $G\alpha_{q/zs}$ (SEQ ID NO: 41).

- 87. The process of any one of claims 36, 37, 38, 39, 43, 55, 67, 68, 71, 72, 76, or 77, wherein the cell is an insect cell.
 - 88. The process of any one of claims 36, 37, 38, 39, 43, 55, 67, 68, 71, 72, 76, or 77, wherein the cell is a mammalian cell.
 - 89. The process of claim 88, wherein the cell is nonneuronal in origin.
- 90. The process of claim 89, wherein the nonneuronal cell is a COS-7 cell, 293 human embryonic kidney cell, a CHO cell, a NIH-3T3 cell, a mouse Y1 cell, or a LM(tk-) cell.
- 91. A process for ident/flying a chemical compound 20 specifically / binds to a which mammalian protein-coupled receptor which comprises contacting cells transfedted with and expressing DNA encoding a chimerac G\ protein and expressing 25 DNA a mammalian G protein-coupled encoding receptor, wherein such cells do not normally express the DNA encoding the chimeric G protein, with the compound ψ n ϕ er conditions suitable for binding, and detecting specific binding of the 30 chemical compound to the mammalian G proteincoupled receptor.
- 92. A process for identifying a chemical compound which specifically binds to a mammalian G protein-coupled receptor which comprises contacting a membrane preparation from cells



15

20

25

30

5

93. A process involving competitive binding identifying а chemical compound which specifically binds to a mammalian G proteinwhich comprises coupled receptor separately contacting cells transfected with and expressing DNA encoding a chimeric G/protein and expressing mammalian G DNA encoding а protein-coupled receptor, wherein such cells do not normally express the DNA encoding the chimeric G protein, with both the chemital compound and a second chemical compound knowh to bind to the mammalian G protein-coupled/feceptor, and with only the chemical / compound under second conditions suitable for b/inding of both compounds, spedific detecting binding ' of the *th*e mammalian \ G protein-coupled to receptor, a dedrease in the binding of the second chemical compound to the mammalian G proteincoupled receptor in the presence of the chemical compound indicating that the chemical compound mammalian G binds to the protein-coupled

35

receptor.

94. A process involving competitive binding for identifying a chemical compound which specifically binds to a mammalian G protein-

which comprises separately coupled receptor a membrane preparation from cells contacting transfected with and expressing DNA encoding a chimeric G protein and expressing DNA encoding a mammalian G protein-coupled receptor, wherein cells do not normally express the DNA encoding the chimeric G protein, with both the chemical compound and a second chemical compound known to bind to the receptor, and with only the chemical compound, under conditions of both compounds, suitable for binding specific binding detecting of the chemical compound the mammalian G protein-coupled to receptor, a decrease in the binding of the second chemical compound to the mammalian G proteincoupled receptor in the presence of the chemical compound indicating /that the chemical compound to the mamma1 G protein-coupled binds an receptor.

20

5

10

15

95. A process of screening a plurality of chemical compounds not known to hind to a mammalian G protein-coupled receptor to identify a compound which specifically binds to the mammalian G protein-coupled receptor, which comprises

25

transfected with contacting cells (a) expressing DNA encoding a chimeric protein and expressing DNA encoding a mammalian G protein-coupled receptor with а compound known to bind specifically to the mammalian G proteincoupled receptor;

35

30

(b) contacting the cells of step (a) with the plurality of compounds not known to

10

15

20

25

30

35

bind specifically to the mammalian G protein-coupled receptor, under conditions permitting binding of compounds known to bind to the mammalian G protein-coupled receptor;

- determining whether the binding of (C) compound known to bind to the mammalian G protein-coupled receptor is reduced in plurality of the presence the compounds, relative to the binding of compound in the absence of the plurality of compounds; and if so
- (d) separately determining the binding to the mammalian G protein-coupled receptor of each compound included in the plurality of compounds, so as to thereby identify any compound included therein which specifically binds to the mammalian G protein coupled receptor.
- 96. A process of screening a pturality of chemical compounds not known to bind to a mammalian G protein-coupled receptor to identify a compound which specifically binds to the mammalian G protein-coupled receptor, which comprises
 - (a) contacting a membrane preparation from cells transfected with and expressing DNA encoding a chimeric G protein and expressing DNA encoding a mammalian G protein-coupled receptor with the plurality of compounds not known to bind specifically to the mammalian G protein-coupled receptor under conditions

10

15

20

permitting binding of compounds known to bind to the mammalian G protein-coupled receptor;

- (b) determining whether the binding of a compound known to bind to the mammalian G protein-coupled receptor is reduced in the presence of the plurality of compounds, relative to the binding of the compound in the absence of the plurality of compounds; and if so
- (c) separately determining the binding to the mammalian G protein-coupled receptor of each compound included in the plurality of compounds, so as to thereby identify any compound included therein which specifically binds to the mammalian G protein-coupled receptor.
- 97. The process of claim 91, 92, 93, 94, 95, or 96, wherein the DNA encoding the mammalian G protein-coupled receptor is endogenous to the cell.
- 98. The process of claim 91, 92, 93, 94, 95, or 96, wherein the DNA encoding the mammalian G protein-coupled receptor is transfected into the cell.
- The process of any one of claims 91, 92, 93, 94, 30 95, 96, wherein the chimeric G or comprises an invertebrate Gaq G protein from which at least five, but not more than twentyone, contiguous amino acids beginning with the Cacid have terminal amino been deleted replaced by a number of contiguous amino acids 35 present in a vertebrate | G protein beginning with

10

15

20

25

the C-terminal amino acid of such vertebrate G protein, wherein such number equals the number of amino acids deleted.

- 100. The process of any one of claims 91, 92, 93, 94, 96, wherein the chimeric G or protein comprises an invertebrate Gaq G protein from which at least five, but not more than twentyone, contiguous amind acids beginning with the C-terminal amino acid have been deleted and replaced by a number of contiguous amino acids present in a vertebrate $G\alpha z$ protein beginning C-terminal amino acid of with the vertebrate Gαz protein, / wherein such number equals the number of $a\min \beta$ acids deleted.
- 101. The process of any one bf claims 91, 92, 93, 94, 95, or 96, wherein , the chimeric G protein comprises an invertebrate Gaq G protein from which at least fave, but not more than twentyone, contiguous/amiho \acids beginning with the Acid\have been deleted C-terminal ami/ho replaced by a/number of contiguous amino acids present in a vertebrate Gαs protein beginning C-terminal amino with the acid of vertebrate Gas/ protein, \wherein such equals the number of amino acids deleted.
- 102. The process of any one of claims 91, 92, 93, 94, 95, or 96 wherein the chimeric G protein comprises an invertebrate Gαq G protein from which at least five, but not more than twenty-one, contiguous amino acids beginning with the C-terminal amino acid have been deleted and replaced by a number of contiguous amino acids

present in a vertebrate $G\alpha i3$ protein beginning with the C-terminal amino acid of such vertebrate $G\alpha i3$ protein, wherein such number equals the number of amino acids deleted.

5

103. The process of any one of claims 91, 92, 93, 94, 95. or 96, wherein the chimeric G protein Caenorhabditis elegans comprises an Gαq protein from which at least five, but not more twenty-one, contiguous amino than acids beginning with the d-terminal amino acid have been deleted and replaced by a number of contiguous amino acids present in a vertebrate G protein beginning with the C-terminal amino acid such vertebrate | G /protein, wherein number equals the number of amino acids deleted.

15

20

25

10

104. The process of any/one of claims 91, 92, 93, 94, 95, or 96, wherein the chimeric G protein comprises a Drosopfila melanogaster Gαq protein, a Limμlus polyphemus Gαq G protein, a Patinopecten yessoensis tag G protein, a Loligo forbesi Gαq G protein a Homarus americanus Gαq G protein, a Lymhaea stagnalis $G\alpha q$ G protein, a Golg ****G ·protein, Geodia cydonium Dictyostelium /discoideum $G\alpha_4$ G protein, which at least five, but not more than twentyone, contiguous amino acids beginning with the C-terminal amino acid have been deleted replaced by a number of contiguous amino acids present in a vertebrate G protein beginning with the C-terminal amino acid of such vertebrate G protein, wherein such number equals the number

of amino acids deleted.

30

10

20

25

- 105. The process of any one of claims 91, 92, 93, 94, 95, or 96, wherein the chimeric G protein has an amino acid sequence substantially the same as the amino acid sequence shown in (a) Figure 2, C. elegans $G\alpha_{q/z5}$ (SEQ ID NO: 1); (b) Figure 2, C. elegans $G\alpha_{q/z9}$ (SEQ ID NO: 2); (c) Figure 2, C. elegans $G\alpha_{q/s9}$ (SEQ ID NO: 3); (d) Figure 2, C. elegans $G\alpha_{q/s9}$ (SEQ ID NO: 4); (e) Figure 2, C. elegans $G\alpha_{q/i3(5)}$ (SEQ ID NO: 5); or (f) Figure 2, D. melaongaster $G\alpha_{q/z5}$ (SEQ ID NO: 41).
- 106. The process of any one of claims 91, 92, 93, 94, 95, or 96, wherein the cell is an insect cell.
- 15 107. The process of any one of claims 91, 92, 93, 94, 95, or 96, wherein the cell is a mammalian cell.
 - 108. The process of claim 7, wherein the cell is nonneuronal in origin.
 - 109. The process of claim 108, wherein the nonneuronal cell is a COS-7 cell, 293 human embryonic kidney cell, a CHO cell, a NIH-3T3 cell, a mouse Y1 cell, of a LM(tk-) cell.
 - 110. The process for making a composition of matter which specifically binds to a mammalian G protein-coupled receptor which comprises identifying a chemical compound using the process of any of claims 36, 37, 43, 67, 71, or 76 and then synthesizing the chemical compound or a novel structural and functional analog or homolog thereof.

- 111. The process for making a composition of matter which specifically binds to a mammalian G protein-coupled receptor which comprises identifying a chemical compound using the process of any of claims 38, 39, 55, 68, 72, or 77 and then synthesizing the chemical compound or a novel structural and functional analog or homolog thereof.
- 112. The process for making a composition of matter 10 specifically binds to which а mammalian G protein-coupled receptor which comprises identifying a chemica‡ compound using process of any of claims 91, 92, 93, 94, 95, or15 96 and then synthesizing the chemical compound or a novel structural and functional analog or homolog thereof.
- 113. The process for preparing a composition which 20 comprises admixing a/ carrier and pharmaceutically effective amount of a chemical compound identified / by the process of any of 37, 71, or 76 or a novel claims 36, 43, structural and functional analog or 25 thereof.
 - 114. The process for preparing a composition which comprises admixing a carrier and a pharmaceutically effective amount of a chemical compound identified by the process of any of claims 38, 39, 55, 68, 72, or 77 or a novel structural and functional analog or homolog thereof.
- 35 115. The process for preparing a composition which comprises admixing a carrier and a

10

15

20

25

30

35

pharmaceutically effective amount of a chemical compound identified by the process of any of 92, 93, claims 91, 94, 95, or 96 a novel or structural and functional analog homolog or thereof.

- 116. A process for determining whether a chemical compound is a ligand for a mammalian G proteinwhich coupled receptor comprises contacting cells transfected with and expressing DNA encoding a chimeric & protein and expressing DNA encoding a mammalian G protein-coupled receptor, with the compound under conditions permitting mammalian G activation of the proteincoupled receptor, and detecting an increase in mammalian G protein-compled receptor activity, so as to thereby determine whether the compound activates mammalian the G protein-coupled receptor and is a //gand for the mammalian G protein-coupled/rece/ptor.
- for determining whether a chemical 117. A process compound is a ligand for a mammalian G proteincoupled receptor which comprises contacting a membrane preparation from cells transfected with and expressing \not DNA encoding a chimeric G protein expressing DNA encoding mammalian protein-couple# receptor, with the compound under conditions permitting the activation of the mammalian G protein-coupled receptor, detecting an increase in mammalian G proteincoupled receptor activity, so as to thereby determine whether the compound activates mammalian G protein-coupled receptor and is a ligand for the mammalian protein-coupled G receptor.

10

15

20

25

30

- 118. A process for determining whether a chemical compound is a ligand for a mammalian G proteincoupled receptor which comprises contacting second messenger response, cells producing a expressing the DNA encoding the mammalian G protein-coupled receptor, and expressing the DNA encoding a chimeric G protein, wherein such cells do not normally express the DNA encoding chimeric the G protein, with the chemical conditions compound under suitable activation of the mammalian G protein-coupled and measuring the second messenger receptor, response in the presence and in the absence of the chemical compound/ a change in the second response In the presence messenger of chemical compound indicating that the compound activates th∉ mammalian G protein-coupled receptor and /is a ligand for the mammalian G protein-coupled redeptor.
- 119. The process of claim 118, wherein the second messenger response is a $G\alpha q$ second messenger response.
- 120. The process of claim 119, wherein the $G\alpha q$ second messenger response comprises intracellular levels calcium and the change in ild messenger an increase in the measure intracellular calcium.
- 121. The process of claim 120, wherein the measure of intracellular calcium levels is made by chloride current readings.

15

20

25

30

- 122. The process of claim 120, wherein the measure of intracellular calcium is made by fluorescence readings, luminescence readings, electrophysiological readings, or through the detection of a reporter protein under the transcriptional control of a calcium-responsive promoter element.
- 123. A process of screening a plurality of chemical compounds not known to activate a mammalian G protein-coupled receptor to identify a ligand for the mammalian G protein-coupled receptor which comprises:
 - transfected contacting cells with (a) and encoding expressing DNA а chimeric protein and expressing DNA encoding a mammalian G protein-coupled receptor with compounds not known to the plurality /of mammalian G protein-coupled activate the receptor, under conditions permitting of. activation mammalian G proteincoupled receptor
 - (b) determining whether the activity of the mammalian G protein-coupled receptor is increased in the presence of one or more of the compounds; and if so
 - determining (C) separately whether the activation of the mammalian G proteincoupled receptor is increased by compound included in the plurality compounds, so as to thereby identify each compound which activates the mammalian G protein-coupled teceptor and is a ligand

10

15

20

25

30

35

for the mammalian G protein-coupled receptor.

124. A process for determining whether a chemical compound is a ligand for a mammalian G proteinreceptor, which comprises separately membrane contacting preparations from transfected with and expressing DNA encoding a chimeric G protein and expressing DNA encoding a mammalian G protein-coupled receptor with both [35]GTPyS, and the compound and with only [35S]GTPyS, conditions under permitting activation of the mammalian G protein-coupled receptor, and detecting [35S]GTPyS binding to the membrane preparation and increase an [35S]GTPYS binding presence in the compound indicating that the chemical compound mammalilary activates the protein-coupled receptor and is a ligard for the mammalian G protein-coupled receptor

125. A process for determining whether a chemical ligand / for compound is а the/ mammalian receptor, protein-coupled which comprises contacting cells transfected with and expressing DNA encoding a chimeric G protein and expressing DNA encodina а mammalian protein-coupled compound, receptor with Vunder conditions act vation permitting the of the mammalian G protein-coupled redeptor, and detecting changes receptor active state conformation manifested by changes in receptor/G protein heterotrimer association/dissociation in presence of the compound indicating that the chemical compound activates the mammalian G

10

15

20

25

30

protein-coupled receptor and is a ligand for the mammalian G protein-coupled receptor.

- identifying a process for ligand for protein-coupled receptor mammalian comprises contacting cells transfected with and expressing DNA encoding a chimeric G protein and expressing DNA encoding a mammalian G proteincoupled receptor, wherein such cells do not normally express the DNA encoding the chimeric G protein, with the dompound under conditions suitable for binding and detecting specific chemical binding of the compound to mammalian G protein-coupled receptor, indicating that the compound is $\frac{1}{4}$ ligand/for the mammalian G protein-coupled receptor.
- 127. A process for identifying a chemical compound dind\$ specifically to a mammalian G protein-coupled receptor which comprises contacting a membrane /preparation from cells transfected with and expressing DNA encoding a chimeric G protein and expressing DNA encoding a mammalian G protein/coupled receptor, wherein such cells do not/ hormally express the encoding the dhimeric G protein, with compound under conditions suitable for binding, and detecting spedific binding of the chemical compound to the / mammalian G protein-coupled receptor, indicating that the compound is a ligand for the mammalian G protein-coupled receptor.
- 128. The process of claim 116, 117, 118, 123, 124, 125, 126, or 127, wherein the DNA encoding the

15

20

25

30

protein-coupled receptor G mammalian is endogenous to the cel1.

- 129. The process of claim 116, 117, 118, 123, 124, 125, 126, or 127, wherein the DNA encoding the protein-coupled receptor mammalian G transfected into the cell.
- 130. The process of any one claims 116, 117, 118, 123, 10 124, 125, 126, or 127 wherein the chimeric G protein comprises an invertebrate Gaq G protein from which at least five, but not more than twenty-one, contiguous amino acids beginning with the C-terminal amino/acid have been deleted and replaced by a number of contiguous amino acids present in a/\vertebrate G beginning with the C-terminal amino acid of such vertebrate G protein, whetein such number equals the number of amino dcids deleted.
 - 131. The process of any one of claims 116, 117, 118, 123, 124, 125, 126, or 127, wherein the chimeric G protein comprises invertebrate Gαq G an protein from which at least fave, but not more than twenty-one, contiguous amino acids beginning with the C-terminal amino acid have been deleted and repladed by a number contiguous amino acids present in a vertebrate Gαz protein beginning with the C-terminal amino acid of such vertebrate $G\alpha z$ protein, wherein such number equals the number of amino acids deleted.
- 132. The process of any one of claims 116, 117, 118, 123, 124, 125, 126, or 127, wherein the chimeric 35

G protein comprises invertebrate $G\alpha\alpha$ G an protein from which at least five, but not more than twenty-one, contiguous amino acids beginning with the C-terminal amino acid have deleted and replaced by a number contiguous amino acids present in a vertebrate Gas protein beginning with the C-terminal amino acid of such vertebrate Gas protein, wherein such number equals the number of amino acids deleted.

133. The process of any one of claims 116, 117, 118, 123, 124, 125, 126, or 127, wherein the chimeric an Invertebrate Gaq G G protein comprises protein from which at least five, but not more twenty-one, contiguous amino beginning with the the minal amino acid have and /teplaced by been deleted a number contiguous amino adids/present in a vertebrate Gi3 protein beginn \not In \not I \not I \not Iith the C-terminal amino acid of such vertebrate Gi3 protein, wherein such number equals the number of amino acids deleted.

134. The process of any one of claims 116, 117, 118, 123, 124, 125, 126, or 127, wherein the chimeric G protein comprises an Caenorhabditis elegans Gaq G protein from which at least five, but not more than twenty-one, contiguous amino acids beginning with the C-terminal amino acid have been deleted and replaced by a number of contiguous amino acids present in a vertebrate G protein beginning with the C-terminal amino acid of such vertebrate G protein, wherein such number equals the number of amino acids deleted.

30

5

10

15

20

25

10

15

135. The process of any one of claims 116, 117, 118, 123, 124, 125, 126, or 127, wherein the chimeric G protein comprises a Drosophila melanogaster Limulus polyphemus $G\alpha q$ GGαq G protein, a Patinopecten yessoensis protein, a Gαq G Loligo forbesi Gaq G protein, protein, a Homarus americanus $G \alpha q$ G protein, a Lymnaea stagnalis Gαq G protein, a Geodia cydonium Gαq G protein, or a Dictyostelium discoideum $G\alpha_4$ G protein, from which at least five, but not more contiguous than twenty-one, amino beginning with the terminal amino acid have replaced by a number of deleted and contiguous amino acids présent in a vertebrate G protein beginning with the C-terminal amino acid such vertebrate G protein, wherein such number equals the number of amino acids deleted.

136. The process of any one of claims 116, 117, 118, 20 123, 124, 125, 1/26, 1/27, wherein the chimeric protein has ah amino acid sequence substantially the same as the amino acid sequence shown in (a) Figure 2, $\sqrt[r]{C}$. elegans G $lpha_{ t q/z5}$ (SEQ ID (b) Figure 2 25 C elegans $G\alpha_{q/z9}$ (SEQ ID NO: 1); $C \setminus elegans G\alpha_{q/s9}$ 2); (c) Figure 2, (SEQ ID C elegans $G\alpha_{q/s21}$ (d) Figure 2, 3); (SEQ ID NO: 4); (e) Figure 2, C. elegans $G\alpha_{g/i3(5)}$ (SEQ ID (f) Figure 2, D. melaongaster $G\alpha_{q/zs}$ or 30 (SEQ ID NO: 41).

137. The process of any one of claims 116, 117, 118, 123, 124, 125, 126, or 127, wherein the cell is an insect cell.

15

20

25

30

- 138. The process of any one of claims 116, 117, 118, 123, 124, 125, 126, or 127, wherein the cell is a mammalian cell.
- 5 139. The process of claim 138, wherein the cell is nonneuronal in origin.
 - 140. The process of claim 139, wherein the nonneuronal cell is a COS-7 cell, 293 human embryonic kidney cell, a CHO cell, a NIH-3T3 cell, a mouse Y1 cell, or a LM(tk-) cell.
 - 141. A process of screening a plurality of independent clones not known to include a clone encoding a mammalian G protein-coupled receptor, to identify and isolate a clone encoding a mammalian G protein coupled receptor, which comprises:
 - contacting /cel/ls\ transferted with (a) expressing AND encoding/ a chimeric protein and expressing DNA encoding bf/ plurality independent clones with a under donditions ligand, permitting activation ϕ f a mammalian G protein-coupled receptor;
 - (b) determining whether the ligand activates the cells expressing the plurality of independent clones and the chimeric G protein; and if so
 - (c) isolating the single clone which expresses the mammalian c protein-coupled receptor activated by the ligand, so as to thereby identify any clone included in the

plurality of clones as encoding a mammalian G protein coupled receptor.

142. A process of screening a plurality of independent clones not known to include a clone encoding a mammalian of protein-coupled receptor, to identify and isolate a clone encoding a mammalian of protein-coupled receptor, which comprises:

10

5

contacting cells transfected with (a) and encoding chimeric G expressing DNA а protein and expressing DNA encoding plurality of independent clones with a /conditions ligand, under permitting specific binding to a mammalian G proteincoupled recept ϕr ;

15

(b) determining whether the ligand specifically binds to the cells expressing the plurality of independent clones and the chimeric G protein; and if so

20

25

(c) isolating the single clone which expresses the mammalian G protein-coupled receptor which specifically binds to the ligand, so as to thereby identify any clone included in the plurality of clones as encoding a mammalian G protein-coupled receptor.

30

143. The process of claim 141 or 142, wherein the DNA encoding the plurality of independent clones is endogenous to the cell.

10

15

20

25

30

35

- 144. The process of claim 141 or 142, wherein the DNA encoding the plurality of independent clones is transfected into the cell.
- 145. The process of claim 141 or 142, wherein the chimeric G protein comprises an invertebrate $G\alpha q$ G protein from which at least five, but not more than twenty-one, contiguous amino beginning with the C-terminal amino acid have replaced by deleted and a number of been contiguous amino acids present in a vertebrate G protein beginning with the C-terminal amino acid & protein, wherein such such vertebrate number equals the number of amino acids deleted.

146. The process of claim |2/41|or 142, wherein the chimeric G protein comprises an invertebrate $G\alpha q$ G protein from which at least five, but not more than twenty-one, contiduous amino acids beginning with the/ C-terminal amino acid have replaced by deleted and a number of contiguous amino acids present in a vertebrate Gaz protein beginning /with the C-terminal amino acid of such verteb f at $G\alpha f$ protein, wherein number such number equals /the of amino acids deleted.

147. The process of claim 11 or 142, wherein the chimeric G protein comprises an invertebrate $G\alpha q$ G protein from which at least five, but not more than twenty-one, contiguous amino acids beginning with the C-terminal amino acid have been deleted and replaced by a number of contiguous amino acids present in a vertebrate $G\alpha s$ protein beginning with the C-terminal amino

10

15

20

25

acid of such vertebrate $G\alpha s$ protein, wherein such number equals the number of amino acids deleted.

- 148. The process of claim 141 or 142, wherein the chimeric G protein comprises an invertebrate Gaq G protein from which at least five, but not more twenty-one, contiguous amino beginning with the C-terminal amino acid have replaced by been deleted and a number contiguous amino acids present in a vertebrate Gαi3 protein beginning with the C-terminal amino acid of such vertebrate Gai3 protein, wherein number of amino acids such number equals the deleted.
 - 149. The process of claim 141 or 142, wherein the chimeric G protein comprises an Caenorhabditis elegans Gaq G protein from which at least five, but not more than twenty-one contiguous amino acids beginning with the C-terminal amino acid have been deleted and replaced by a number of contiguous amino acids present in a vertebrate G protein beginning with the C-terminal amino acid of such vertebrate G protein, wherein such number equals the number of amino acids deleted.
- 150. The process of 141 or 142, wherein the chimeric G protein comprises a Prosophila melanogaster

 30 Gαq G protein, a Limulus polyphemus Gαq G protein, a Patinopecten yessoensis Gαq G protein, a Loligo forbesi Gαq G protein, a Homarus americanus Gαq G protein, a Lymnaea stagnalis Gαq G protein, a Geodia cydonium Gαq G protein, or a Dictyostelium discoideum Gα4 G

25

5

protein, from which at least five, but not more than twenty-one, contiguous amino acids beginning with the C-terminal amino acid have been deleted and replaced by a number of contiguous amino acids present in a vertebrate G protein beginning with the C-terminal amino acid of such vertebrate G protein, wherein such number equals the number of amino acids deleted.

- 151. The process of clai $\frac{1}{1}$ 141 or 142, wherein the 10 chimeric G protein has an amino acid sequence substantially the same as the amino acid sequence shown in (a) Figure $\c 2$, $\c C$. elegans $\c Glpha_{q/z5}$ (SEQ ID NO: 1); (b) Figure 2, C. elegans $G\alpha_{q/z9}$ (SEQ ID 15 NO: 2); (c) Figure 2, C_r elegans $G\alpha_{q/s9}$ (SEQ ID $/\!\!/ C$. elegans $G\alpha_{q/s21}$ (SEQ ID NO: 3); (d) Figure 21 NO: 4); (e) Figure 2, C. elegans $G\alpha_{g/i3(5)}$ (SEQ ID NO: 5); or (f) Fig/me 2, D. melaongaster $G\alpha_{g/zs}$ (SEQ ID NO: 41).
 - 152. The process of claim 141 or 142, wherein the cell is an insect cell.
 - 153. The process of claim 141 or 142, wherein the cell is a mammalian cell.
 - 154. The process of claim 153, wherein the cell is nonneuronal in origin
- 30 155. The process of claim 154, wherein the nonneuronal cell is a COS-7 cell, 293 human embryonic kidney cell, a CHO cell, a NIH-3T3 cell, a mouse Y1 cell, or a LM(tk-) cell.